Attached hereto is a marked up version of the changes made. The attached page is captioned "**Marked Version to Show Changes Made.**"

REMARKS

Previously pending claims 1, 18-19 and 22-23 are herein amended. New claims 31-36 are added herein. Claims 1-36 are thus pending and presented to the Examiner for examination.

Applicants respectfully direct the attention of the Examiner once more to the pendency of this application and the following co-pending patent applications that were all filed on the same day, February 12, 2001, and again identified herein:

- Serial No. 09/782,168 (Injectable Pharmaceutical Composition Comprising Coated Particles of Camptothecin) – NOTICE OF ALLOWANCE MAILED 9/18/02 (Examiner Azpuru-Unit 1615)
- Serial No. 09/782,167 (Method for Administering Camptothecins Via Injection of a Pharmaceutical Composition Comprising Coated Particles of a Camptothecin) – NOTICE OF ALLOWANCE MAILED 8/7/02 (Examiner Azpuru-Unit 1615)
- Serial No. 09/782,184 (Injectable Pharmaceutical Composition Comprising Microdroplets of a Camptothecin) – *CURRENTLY PENDING*
- Serial No. 09/782,182 (Method for Administering Camptothecins Via Injection of a Pharmaceutical Composition Comprising Microdroplets of a Camptothecin) – NOTICE OF ALLOWANCE MAILED 8/7/02 (Examiner Azpuru-Unit 1615)

CONCLUSION

It is submitted that the present application is in form for allowance, and such action is respectfully requested. Should the Examiner have any questions, please contact the undersigned attorney.

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. 23-2415 (Docket No. 12636-898).

Respectfully submitted,

WILSON SONSINI GOODRICH & ROSATI

Date: 11/13/02

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In re application of: Howard Sands, et al.
Application No.: 09/782,184
Filed: February 12, 2001
Title: Injectable Pharmaceutical Composition Comprising Coated Particles of Camptothecin

MARKED VERSION TO SHOW CHANGES MADE

1. (Twice Amended) An injectable pharmaceutical composition comprising:

an aqueous suspension of microdroplets suitable for intravenous delivery, the microdroplets having a mean diameter between 200 Angstroms and one micron, the microdroplets comprising a substantially water-insoluble, pharmacologically acceptable liquid that does not tend to form micelle structures, a camptothecin ~~9-nitro-20(S)-camptothecin~~ dissolved in water-insoluble, and pharmacologically acceptable liquid ~~that are positioned within~~, and an outer layer comprising ~~of the microdroplet that comprises~~ a phospholipid.

18. (Twice Amended) An injectable pharmaceutical composition comprising:

a dispersion in an aqueous carrier solution comprising one or more pharmaceutically acceptable tonicity modifier agents and liquid droplets having a size range of micrometer to submicrometer, the droplets comprising

~~at least one membrane-forming amphipathic lipid that forms an outer layer of a given droplet,~~

a substantially water-insoluble, pharmaceutically acceptable lipophilic liquid vehicle with at least one membrane-forming lipid that does not tend to form micelle structures and a camptothecin dissolved in the lipophilic liquid vehicle, and

~~9-nitro-20(S)-camptothecin dissolved in the lipophilic liquid vehicle,~~

an outer layer surrounding the droplet comprising at least one membrane-forming amphipathic lipid,

~~where the lipophilic liquid vehicle and the solid particles of the camptothecin are positioned within the outer layer of the given droplet;~~

wherein upon thermal sterilization the dispersion does not aggregate, flocculate, agglomerate, or coalesce, and the droplets do not grow in size above a volume weighted mean diameter of 10 μm.

19. (Twice Amended) An injectable pharmaceutical composition comprising:

an aqueous carrier solution comprising one or more pharmaceutically acceptable tonicity modifier agents;

a dispersion of liquid droplets of a first size distribution~~having a size range of submicrometer to micrometers~~, the liquid droplets comprising

~~at least one membrane-forming amphipathic lipid that forms an outer layer of a given droplet,~~

a substantially water-insoluble, pharmaceutically acceptable lipophilic liquid vehicle that does not tend to form micelle structures, ~~and~~

solid particles of a camptothecin of a second size distribution~~9-nitro-20(S)-camptothecin~~, and

an outer layer surrounding the droplet comprising at least one membrane-forming amphipathic lipid;

~~—~~wherein the first size distribution is in the range of submicrometer to micrometers, and the second size distribution is smaller than the first size distribution; and ~~where the lipophilic liquid vehicle and the solid particles of the camptothecin are positioned within the outer layer of the given droplet;~~

wherein upon thermal sterilization, the dispersion does not aggregate, flocculate, agglomerate, or coalesce, and the droplets do not grow in size above a volume weighted mean diameter of 10 μm.

22. (Amended) An injectable pharmaceutical composition according to claim 20 wherein the phospholipid is selected from the group consisting of natural and synthetic lipids, hen egg-derived phospholipid, egg phospholipid, purified egg phospholipid, soy phospholipid, dimyristoyl lecithin, didodecanoyl lecithin, dioeoyl lecithin, dilinoeoyl lecithin, alpha-palmito-beta-oleoyl lecithin, alpha-palmitoyl-beta-linoleoyl lecithin, alpha-oleoyl-beta-palmitoyl lecithin, diarachidonyl lecithin, alpha-palmito-beta-myristoyl lecithin, dimyristoyl phosphatidic acid, dipalmitoyl phosphatidic acid, distearoyl phosphatidic acid, phosphatidyl serine, phosphatidyl inositol, dimyristoyl phosphatidyl glycerol, dipalmitoyl phosphatidyl glycerol, dioctadecanoyl phosphatidyl ethanolamine, dioleoyl phosphatidyl ethanolamine, dihexadecyl phosphatidyl ethanolamine, dilauryl phosphatidyl ethanolamine, dimyristoyl

phosphatidyl ethanolamine~~,~~ and~~-~~ dipalmitoyl phosphatidyl ethanolamine~~, Lipoid E80, Lipoid ES, Lipoid 90H, and Lipoid 100H~~.

23. (Amended) An injectable pharmaceutical composition according to claim 20 wherein the phospholipid comprises egg phospholipid~~Lipoid E80~~.